Osteomyelitis

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Objectives

- Be familiar with factors that may lead to osteomyelitis
- Be familiar with complications of vertebral osteomyelitis
- Discuss diabetic foot infections
- Discuss osteomyelitis complicating sacral pressure ulcers
- Understand the role of biofilm in prosthetic joint infections (PJI)
- Briefly discuss DAPITO and OVIVA trials for duration and modality of treatment

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How does it happen?

- Hematogenous seeding
  - Vertebral osteomyelitis, Long bones (kids)
- Continguous spread
  - Open wound; diabetic foot infection
- Direct Inoculation
  - Trauma or surgery

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Classification by time of onset

- Acute: within 2 weeks of infection
- Subacute: within 1-2 months of infection
- Chronic: >2 months of infection

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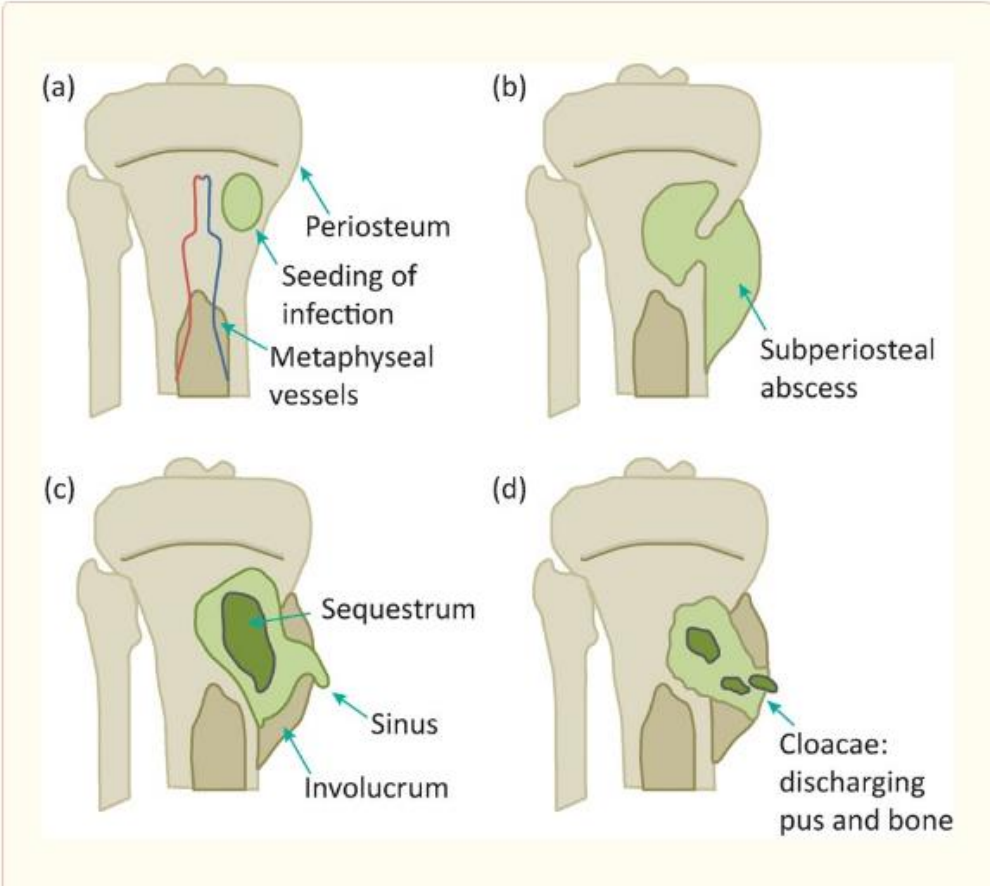
Pathogenesis of Osteomyelitis



Colston et al. Clinical Medicine, 2018.

Host factors for Osteomyelitis

- Poorly controlled Diabetes
  - Decreased response to infection and bacterial proliferation
- Peripheral vascular disease
  - Local ischemia
- Substance use disorder (injection drug use)
- Sickle cell disease
  - Impaired gut defense

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Question:

Which of the following is most true about acute or sub-acute osteomyelitis?

a. It is typically treated with 4-weeks of antibiotics
b. Diagnosis can be made by x-ray 7-14 days after infection
c. Cure can only be achieved with IV antibiotics
d. The most common bacterial cause is *Staphylococcus aureus*

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Why is *S. aureus* the most common cause?

- Pathogenicity
- Sticky

	6-week regimen (n=176)	12-week regimen (n=175)	Total (n=351)
Microbiological diagnosis			
Blood culture	119 (68%)	121 (69%)	240 (68%)
CT-vertebral biopsy	67 (38%)	71 (41%)	138 (39%)
Perioperative surgical biopsy	9 (5%)	10 (6%)	19 (5%)
Microbiological identification			
Staphylococcus aureus†	69 (39%)	76 (43%)	145 (41%)
Coagulase-negative *Staphyloccocus*‡	29 (16%)	32 (18%)	61 (17%)
Streptococcus spp	32 (18%)	31 (18%)	63 (18%)
Enterococcus spp	11 (6%)	15 (9%)	26 (7%)
Enterobacterial spp	22 (13%)	16 (9%)	38 (11%)
Anaerobia	7 (4%)	6 (3%)	13 (4%)
Other Gram-negative bacteria	6 (3%)	4 (2%)	10 (3%)
Other *Streptococcus*	4 (2%)	4 (2%)	8 (2%)

Bernard et al. Lancet 2015.

Question:

In a patient with thoracic vertebral osteomyelitis

a. CT scans are highly sensitive for diseases of the spinal cord
b. If there is a history of back pain or injury, this decreases the likelihood of osteomyelitis as the diagnosis
c. An epidural abscess is a medical emergency b/c the spinal cord may be irreversibly compressed and infarcted
d. Complete paralysis for greater than 3 days is an indication for surgery

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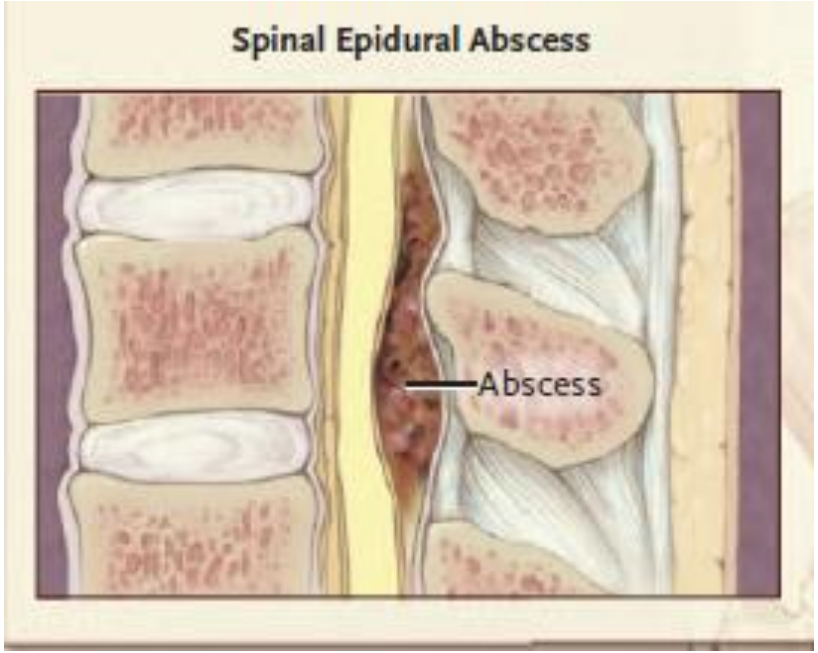
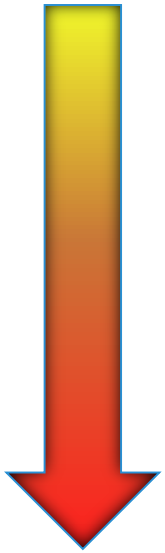
Spinal Epidural Abscess

- Often rupture posteriorly into epidural space
- Typically extend 3-4 vertebrae



Darouiche, NEJM. 2006.

Staging of symptom progression



- Back pain at affected spinal level
- Nerve root pain radiating from involved spinal areas
- Nerve dysfunction: weakness, lost sensation, bowel and bladder dysfunction
- Paralysis

Davis et al. J Emer Med. 2004.

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Staging of symptom progression

Table 6. Comparison Between Patients with and without Diagnostic Delay with Regard to Clinical Presentation and Neurologic Outcome

Parameter	Patients with Diagnostic Delay (n = 47)	Patient without Diagnostic Delay	Odds Ratio
% of all patients	75		N/A
Multiple ED visits (%)	68		N/A
Admission delay (%)	66		N/A
Neurologic deterioration during "delay" (%)	57		N/A
"Classic triad" present at admission (%)	9	13	0.65 (0.11–3.95)
Residual weakness at discharge (%)	45	13	5.7* (1.2–27.7)

68% in dx delay group had h/o IVDU

* $p < 0.05$.

Darouiche, NEJM. 2006.
Davis et al. J Emer Med. 2004.

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Question:

In patients with DM and chronic osteomyelitis of the foot, medical management with antibiotics alone is difficult b/c:

a. It's likely caused by a highly resistant bacteria
b. The infected tissue likely has impaired vascular supply and thus impaired antibiotics and immune cell delivery
c. Patients with diabetes may not be able to complete full courses of treatment
d. These infections are often polymicrobial so it is difficult to find antibiotics to cover all organisms that grow in culture

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Diabetic foot infections

- Commonly through **contiguous/local spread**
- Metatarsal head and heel
- MRI most helpful imaging modality
- Culture yield is increased if **off antibiotics at least 48 hours**

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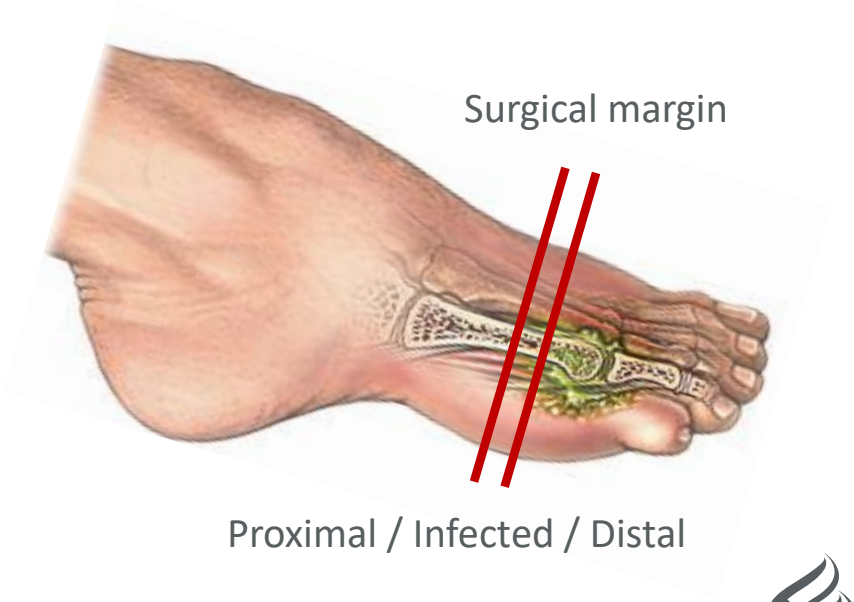
Importance of cultures

- Typically polymicrobial
  - Certain bacteria make difference in treatment
- **Source control** is critical for cure
  - Surgical margin cultures
  - Surgical pathology



Lipsky et al. CID, 2012.
Image: A.D.A.M.

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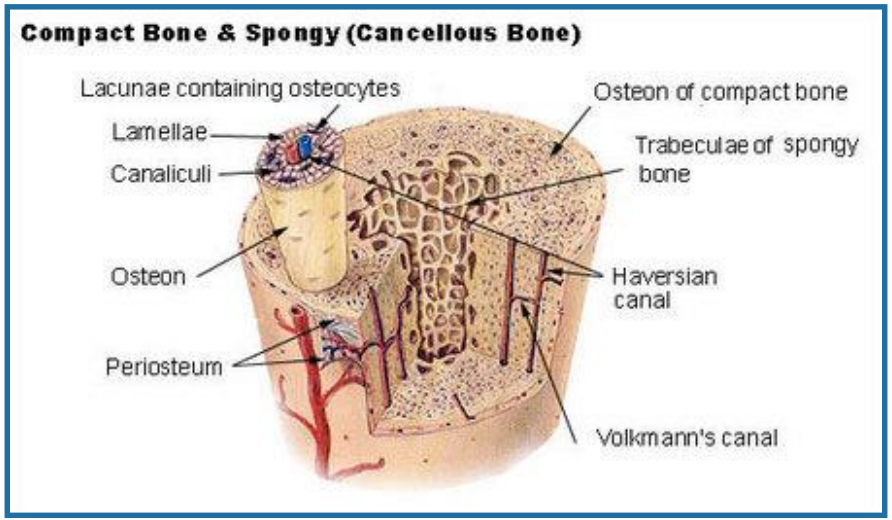
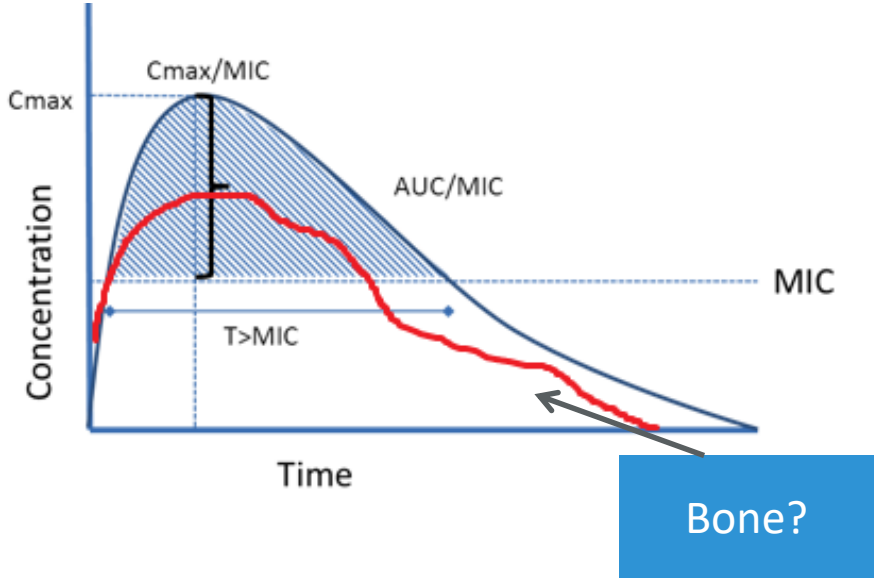
Blood supply matters





Slide credit: Luke Strnad,MD

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Question:

In a patient with a sacral pressure ulcer, if bone is exposed:

a. Empiric vancomycin + piperacillin/tazobactam should be initiated
b. This is diagnostic of osteomyelitis
c. MRI will be most helpful in diagnosis of osteomyelitis
d. Bone biopsy after debridement would be necessary to establish a diagnosis of osteomyelitis

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Osteomyelitis and Sacral Pressure Ulcers

- Exposed bone **does not always mean** osteomyelitis
  - Biopsy after debridement to make diagnosis
- Role of imaging limited by variable specificity
- If osteomyelitis, no data to support antibiotics without plan for covering wound

Wong et al. CID 2019.

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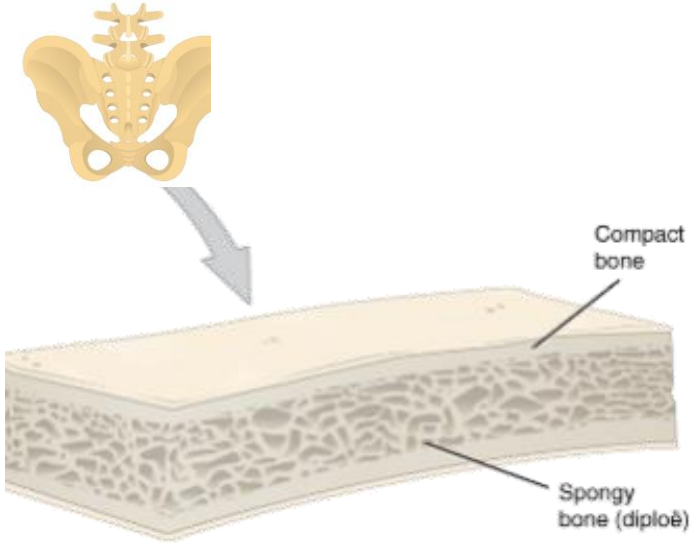
Osteomyelitis and Sacral Pressure Ulcers

- Duration of treatment:
  - Restricted to superficial bony cortex = 2 weeks
  - Medullary bone = 4-6 weeks



Wong et al. CID 2019.

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Question:

62 y/o male w/progressive R hip pain 7 months after R THA. The pain started 4 wks after surgery. On exam, has pain on external rotation of the right hip. X-ray shows loosening of the prosthesis. CBC, ESR, & CRP are normal.

a. The normal labs and lack of systemic symptoms rule out infection

b. Coagulase negative *staphylococci* is the most likely cause of his pain

c. The loosening on x-ray is diagnostic of a late infection

d. A hip incision and drainage with prosthesis retention would provide optimal chance of cure

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Prosthetic joint infection & Periprosthetic Osteomyelitis

Organism	All	Late PJI (> 12 months implant) (n=182)
S. aureus	21-43%	13.1%
Coag-neg staphylococci	17-39%	33.9%
Streptococci	7-12%	
Enterobacteriaceae	5-12%	
Enterococci	1-8%	
Anaerobic bacteria	2-6%	17.6 %(*C. Acnes*)

*Cutibacterium acnes makes up 3% of hip/knee PJI, but 38% of shoulder PJI

Mandell et al. 2015.
Triffault-Fillit et al. Clin Microbiol Inf 2019.

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When to suspect PJI?

- Acute onset of pain of prosthetic joint
- Chronic painful prosthesis at any time after prosthesis implantation
- Sinus tract or persistent wound drainage
- History of prior wound healing problems or superficial or deep infection

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Question:

Which is most true: In a patient with a prosthetic joint infection (PJI) that develops 6 months after surgery:

a. The infection in the joint likely occurred in the prior 3-4 weeks
b. Aspirate cultures are highly sensitive in making the diagnosis
c. Cure rates are similar with hardware removal and retention, but antibiotic duration differs
d. Cure is dependent on removing the bacteria in the biofilm

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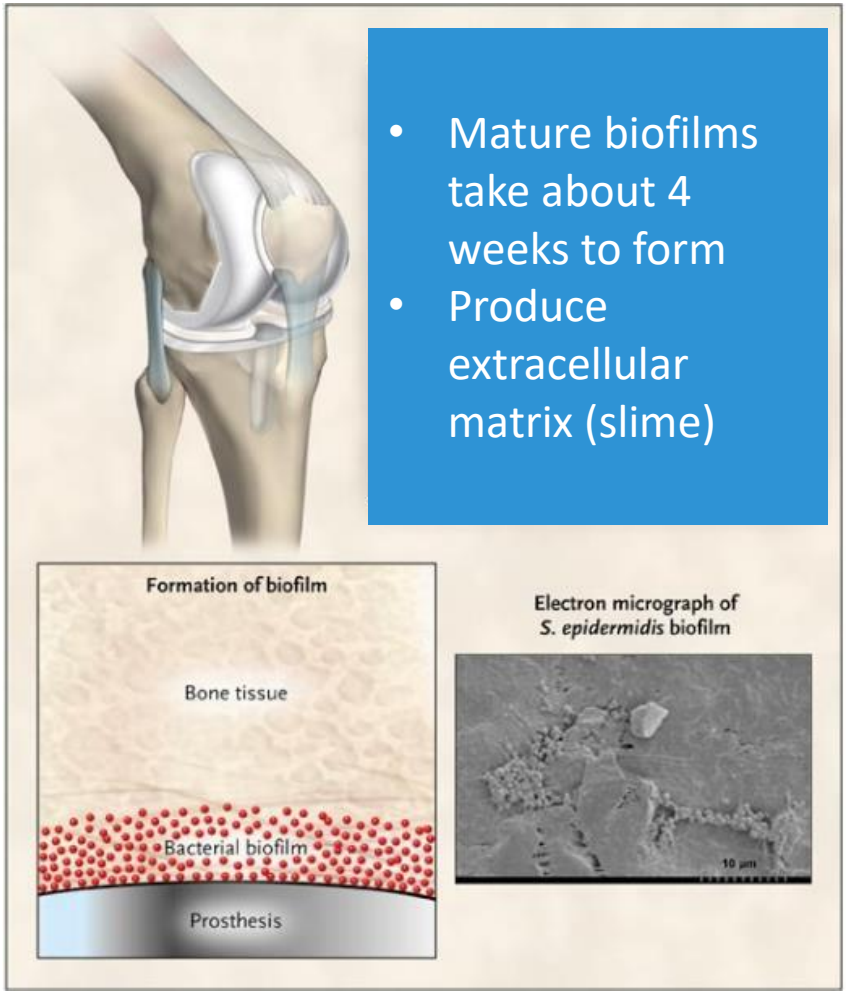
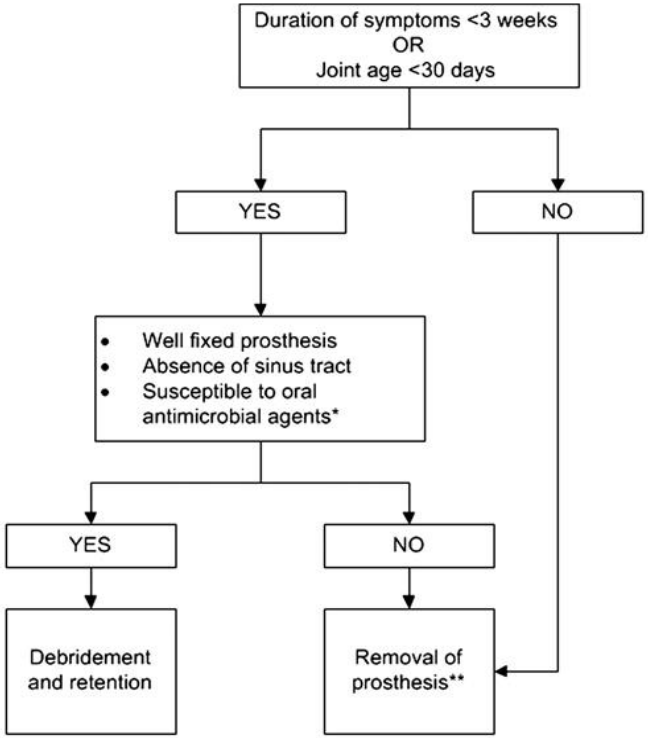
What is biofilm?

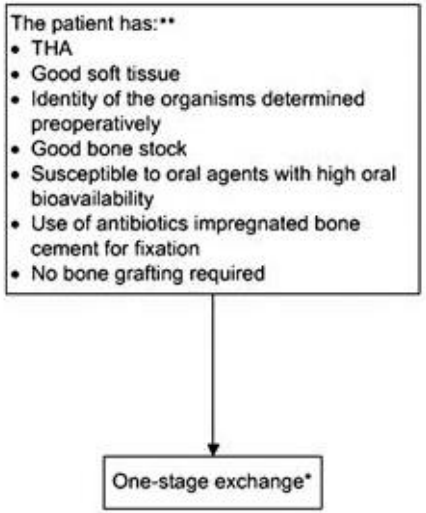
- Chronic hardware infections difficult to cure without removal/explant
- **Need Source Control!**

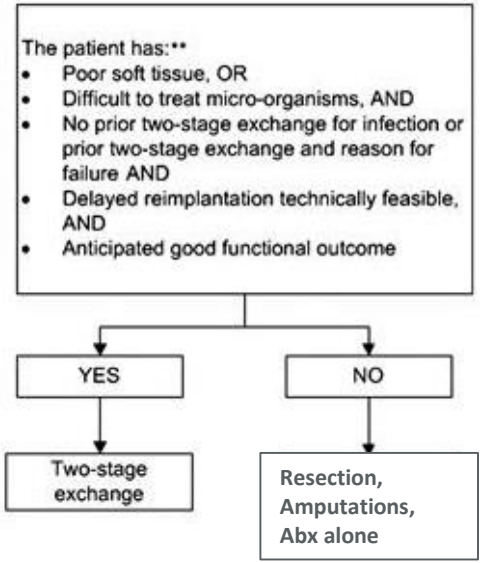


Pozo et al. NEJM, 2009.

IDSA PJI Guidelines







Osmon et al. CID, 2013.

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DAIR – Risk factors for failure

- Successful in 52-65% of hip and knee PJI
- Increased failure:
  - Longer duration since primary arthroplasty
  - Increased CRP at diagnosis
  - *S. aureus* and Gram negative organisms

Zhu et al. J of Arthroplasty, 2021.

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DATIPO Trial: Duration of Antibiotic Treatment in PJI

- Multicenter, open-label, randomized controlled noninferiority trial
- Primary end point: persistent infection within 2 yrs of end of abx
  - 6 weeks: 18.1% 12 weeks: 9.4%
- 8.7 difference in risk (95% CI, 1.8 to 15.6)
  - **Did not** meet criterion for non inferiority
- No significant difference in AEs: C.diff, Length of stay, Functional outcomes

Bernard et al. NEJM, 2021.

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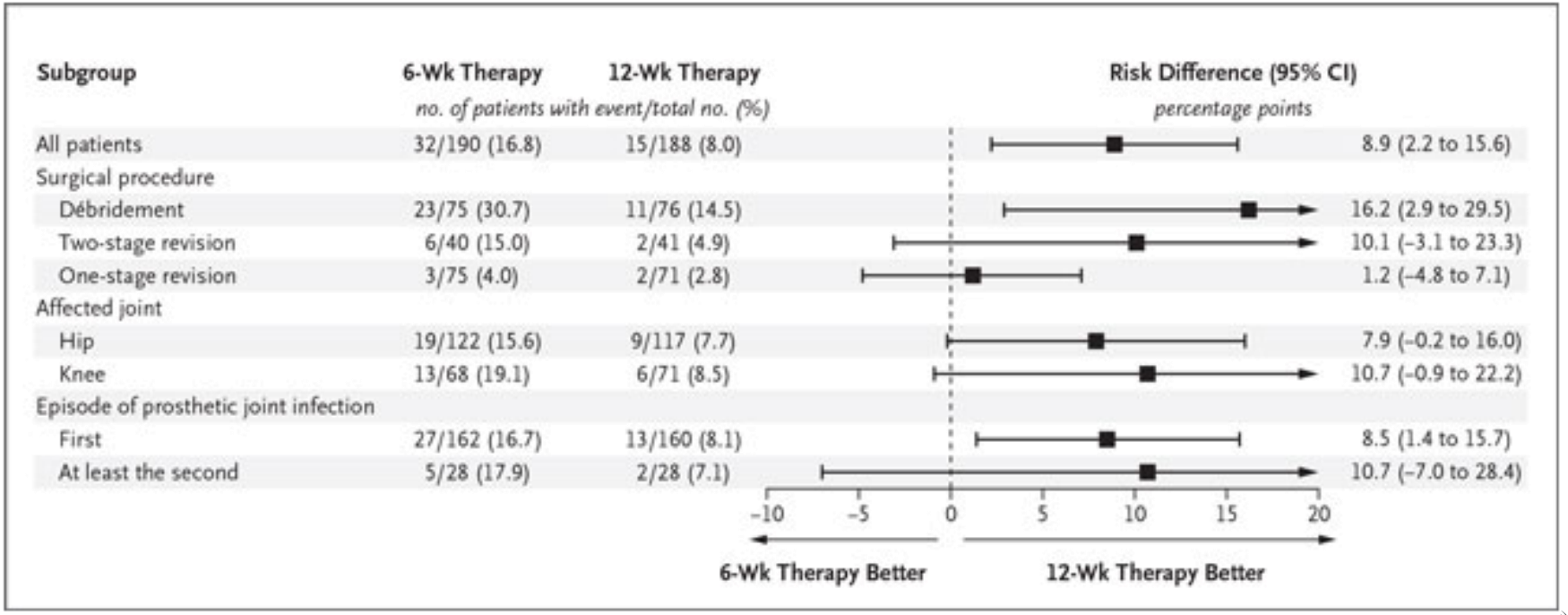

Bernard et al. NEJM, 2021.

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Antibiotics and route

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline and Antibiotic Treatments during the Trial.*

Characteristic	6-Wk Therapy (N=203)	12-Wk Therapy (N=201)
Antibiotic treatment		
Median duration of intravenous administration (IQR) — days¶¶	9 (5–15)	9 (5–15)
≥1 Oral antibiotic agent — no./total no. (%)‖‖	191/203 (94.1)	189/201 (94.0)
Rifampin	144/191 (75.4)	123/189 (65.1)
Quinolone	137/191 (71.7)	123/189 (65.1)
Clindamycin	35/191 (18.3)	52/189 (27.5)
Trimethoprim–sulfamethoxazole	22/191 (11.5)	34/189 (18.0)
Amoxicillin with or without clavulanic acid	19/191 (9.9)	21/189 (11.1)

Bernard et al. NEJM, 2021.

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Question:

You are counseling a patient on treatment of their osteomyelitis, which is most true:

a. After surgical debridement, IV antibiotics for 4-6 weeks are best to achieve cure
b. 2-5 days of antibiotics is adequate after surgery
c. A long acting injectable antibiotic like dalbavancin should not be considered in any situation
d. Oral antibiotics may be a possible treatment option depending on the susceptibilities of the infecting organism and the bioavailability of the potential antibiotic

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Oral V IV Antibiotics for Bone and Joint Infections: OVIVA

- *Inclusion criteria:*
  - Native osteomyelitis of extra-axial skeleton, Native joint infection requiring excision arthroplasty, PJI/Orthopedic fixed-device infection, Vertebral osteomyelitis with or without associated diskitis or soft tissue infection, Surgery and no surgery
- *"Pragmatic"*: **ID physician** picked which antibiotic (IV or Oral) once assigned
- Treatment success at 1 year about 86% **irrespective of treatment route**

Li HK et al. NEJM, 2019.

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Surgical management common in OVIVA – Source control!

Table 1. Baseline Characteristics of the Trial Participants.*

Characteristic	Intravenous Group (N=527)	Oral Group (N=527)	Total (N=1054)
Age — yr			
Median (interquartile ra		70)	60 (49–70)
Range		1	18–92
Male sex — no. (%)		7.9)	678 (64.3)
Baseline surgical procedure			
No implant or device present; débridement of chronic osteomyelitis performed	153 (29.0)	169 (32.1)	322 (30.6)
No implant or device present; débridement of chronic osteomyelitis not performed	25 (4.7)	29 (5.5)	54 (5.1)
Débridement and implant retention	124 (23.5)	123 (23.3)	247 (23.4)
Removal of orthopedic device for infection	89 (16.9)	78 (14.8)	167 (15.8)
Prosthetic joint implant removed	68 (12.9)	67 (12.7)	135 (12.8)
Prosthetic joint implant, one-stage revision	47 (8.9)	43 (8.2)	90 (8.5)
Surgery for diskitis, spinal osteomyelitis, or epidural abscess; débridement performed	8 (1.5)	5 (0.9)	13 (1.2)
Surgery for diskitis, spinal osteomyelitis, or epidural abscess; débridement not performed	13 (2.5)	13 (2.5)	26 (2.5)

Only 7.6% did not have some sort of surgical intervention

Li HK et al. NEJM, 2019.

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OVIVA: Antibiotics Selected

Oral antibiotics: known to have good bio- availability:

- Quinolones
- Clindamycin
- Tetracycline
- Combination (Cipro + doxy/clinda)

	Participants randomized to IV Antibiotic* (N = 521)	Participants randomized to PO Antibiotic* (N = 523)	Total* (N = 1044)
Glycopeptides[a] (IV)	214 (41.1%)	22 (4.2%)	236 (22.6%)
Penicillins (IV)	38 (7.3%)	11 (2.1%)	49 (4.7%)
Cephalosporins (IV)	173 (33.2%)	8 (1.5%)	181 (17.3%)
Carbapenems (IV)	41 (7.9%)	5 (1.0%)	46 (4.4%)
Other single IV antibiotic	35 (6.7%)	2 (0.4%)	37 (3.5%)
Combination IV antibiotics	35 (6.7%)	6 (1.1%)	41 (3.9%)
Penicillins (PO)	8 (1.5%)	83 (15.9%)	91 (8.7%)
Quinolones[b] (PO)	33 (6.3%)	191 (36.5%)	224 (21.5%)
Tetracyclines[c] (PO)	4 (0.8%)	57 (10.9%)	61 (5.8%)
Macrolides / Lincosamide [d] (PO)	10 (1.9%)	68 (13.0%)	78 (7.5%)
Other single PO antibiotic (PO)	10 (1.9%)	54 (10.3%)	64 (6.1%)
Combination PO antibiotics (PO)	13 (2.5%)	87 (16.6%)	100 (9.6%)

Li HK et al. NEJM, 2019.

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Take home points:

- Blood supply and source control are essential to treating osteomyelitis
- Most biofilms need surgical management
- Exposed bone in a sacral pressure ulcer does not automatically mean osteomyelitis
- Oral antibiotics can be used, especially in setting of good source control

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Thank You

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